THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte K. OPITZ

Appeal No. 94-4129
Application 07/953,439[1]

ON BRIEF

Before WINTERS, SCHAFER, and GRON, Administrative Patent Judges.

GRON, Administrative Patent Judge.

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[1] Application for patent filed September 29, 1992. According to applicant, this application is a continuation of Application 07/675,835, filed March 27, 1991, now abandoned. Applicant also claims the benefit under 35 U.S.C. § 119 of the March 29, 1990, filing date of Federal Republic of Germany Application P 4010079.0.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

1. Introduction

This is an appeal from an examiner's rejection of Claims 16-19. Nonelected Claims 11-15 and 20 have been withdrawn from further consideration by the examiner in accordance with 37 CFR § 1.142(b). Claims 16-19 stand finally rejected under 35 U.S.C. § 103 as being unpatentable in view of the combined teachings of Davis, U.S. 4,663,318 (patented May 5, 1987), and Bundesrepublik Deutschland Patentschrift DE 3,843,239 (published February 22, 1990). Though the examiner named the German patent publication as the basis for the rejection, both the examiner and appellant have throughout the prosecution of this application liberally referred to its U.S. counterpart, Hille et al. (Hille I), U.S. 5,089,267 (patented February 18, 1991; prior art under 35 U.S.C. § 102(e) based on its U.S. filing date of December 18, 1989), as the English translation. So shall we.

Appellant cites Wislicki, "Nivalin (Galanthamine Hydrobromide), An Additional Decurarizing Agent, Some Introductory Observations," British Journal of Anaesthesia,

Volume 39, pages 963-968 (1967), for the proposition that "galanthamine has only one tenth of the activity of neostigmine which has the same activity as physostigmine" (Brief on Appeal, page 7, second full paragraph). While we find in Wislicki a statement that "the potency of neostigmine [as an anesthetic] is considered to be ten times as great [as] . . . galanthamine" (Wislicki, page 965, column 2, last paragraph), we cannot find a statement that "neostigmine . . . has the same activity as physostigmine" anywhere in Wislicki or in the specification. To the contrary, appellant's specification teaches at pages 4-5, bridging paragraph):

> Due to its pharmacological properties galanthamine belongs to the group of the reveribly [sic, reversibly] acting cholinesterase inhibitors. The effects of galanthamine are similar to those of physostigmine and neostigmine, however, it has additional special effects. The therapeutic range of galanthamine is 3 to 6 times larger than that of physostigmine or neostigmine, because of its lower toxicity (Paskov, D.S., ed. Springer-Verlag, Berlin - Heidelberg - New York - Tokyo, 653-672 (1986).

Moreover, the specification also teaches at page 5:

> In contrast to neostigmine, galanthamine overcomes the blood-brain barrier and opposes the cerebral effect of cholinergic poisons. Galanthamine has the effect of awakening the patient from the twilight sleep caused by scopolamine (Baraka, . . . J. Amer. Med. Assoc. 238, 2293-2294 (1977).

> Due to the long duration of action, galanthamine, which incorporates the properties of physostigmine and neostigmine, is a valuable agent in anesthesiology, since many patients suffer from a central anticholinergic syndrome after a general anaesthesia (Cozanitis, . . . Anaesthesist 26, 649-650 (1977).

The claims on appeal are directed to a transdermal applicator comprising (a) an impermeable backing layer, (b) a polymer matrix which contains galanthamine and is connected to the backing layer, and (c) a pressure-sensitive adhesive element for affixation to the skin. Claim 16, which is representative of the claimed subject matter, is reproduced in the attached Appendix.

We hereby cite for the first time Hille et al. (Hille II),
U.S. 5,700,480, patented December 23, 1997 (copy attached), which issued from Application 08/495,609, filed September 29, 1995. Hille II and this application appear to be commonly assigned to LTS Lohman Therapie-Systeme GmbH & Co. KG. Hille II claims a transdermal therapeutic system for therapeutic administration of galanthamine comprising (a) an impermeable backing layer, (b) a polyacrylate reservoir which contains galanthamine and is connected to the backing layer, and (c) a pressure-sensitive adhesive element for affixation to the

skin. As in this case, both Davis and Hille I are included in the References Cited in Hille II. We find in Hille I an express teaching that the reservoir layer of a transdermal applicator for administering physostigmine may include a polyacrylate matrix. Also, we take particular notice of two statements in Hille II. First, at column 1, lines 26-27, Hille II states, "Lately, galanthamine has been used in the treatment of alcohol dependence (Opitz, K., DE 40 10 079)." Second, at column 1, lines 40-55, Hille II states:

> Accordingly, it is the object of the present invention to provide galanthamine . . . in the form of a transdermal therapeutic system which releases galanthamine . . . over a period of at least 24 hours in a controlled manner . . . .
>
> With the present invention this object is achieved in a surprising manner by a transdermal therapeutic system.
>
> This solution is remarkable all the more since the structure of galanthamine is very similar to that of the opiates. Opiates are considered to be a substance class which only insufficiently penetrates human skin.

2. Findings

A. Galanthamine is useful in treating Alzheimer's Disease (Davis, column 1, lines 6-8).

B. Galanthamine may be administered to treat Alzheimer's Disease

(a) orally in solution, tablet or capsule form,

(b) subcutaneously or intravenously by injection, or

(c) intracerebroventricularly by implanted reservoir (Davis, column 1, line 60, to column 2, line 44).

C. Physostigmine is useful in treating Alzheimer's Disease (Hille, column 1, lines 10-13);

D. Physostigmine may be administered to treat Alzheimer's Disease transdermally via an applicator comprising (a) an impermeable backing layer, (b) a polymer matrix which contains physostigmine and is connected to the backing layer, and (c) a pressure-sensitive adhesive element for affixation to the skin (Hille I, column 1, line 58, to column 3, line 26).

E. Galanthamine and physostigmine have significantly different molecular formula, structural formula, melting points, and solubility characteristics (Brief on Appeal, page 6, citing The Merck Index, Tenth Edition, Merck & Co., Inc.,
pages 620 and 1061-1065 (1983); see also Davis, column 1, line 67, to column 2, line 2).

F. Galanthamine, physostigmine, and neostigmine are known reversibly acting cholinesterase inhibitors with similar

effects. However, galanthamine has additional special effects due to its lower toxicity (Specification, pages 4-5, bridging paragraph).

G. Galanthamine is ten times less potent as an anesthetic than neostigmine (Wislicki, page 965, column 2, last paragraph).

H. The evidence of record does not establish the relative activities of galanthamine to physostigmine for any purpose, of galanthamine to neostigmine for uses other than anesthesia, and of physostigmine to neostigmine for any utility.

I. In 1994, Hille II teaches that he considered the discovery that galanthamine could be administered transdermally remarkable “since the structure of galanthamine is very similar to that of the opiates. Opiates are considered to be a substance class which only insufficiently penetrates human skin” (Hille II, column 1, lines 52-55).

J. The evidence of record does not establish whether or not or the reasons why persons having ordinary skill in the art might reasonably expect a known active agent to be effectively administrable transdermally.

3. Discussion

"A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art . . . ." 35 U.S.C. § 103. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), teaches, 837 F.2d at 1074, 5 USPQ2d at 1598:

> The PTO has the burden under section 103 to establish a *prima facie* case of obviousness. . . . It can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.

The consistent criterion for determining obviousness under 35 U.S.C. § 103 is whether the prior art would have reasonably suggested the claimed invention to one of ordinary skill in the art with reasonable expectation of achieving success. To resolve the issue, the full field of the invention must be considered. The person having ordinary skill is charged with knowledge of the entire body of technological literature, including that which leads to and that which leads away from the claimed invention. In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988).

Assuming that the evidence before us represents the full field of the invention and the entire body of technological literature to be considered by persons having ordinary skill in the art in determining unpatentability under 35 U.S.C. § 103, we must reverse the examiner's holding. We find no evidence in the prior art which would have led persons having ordinary skill in the art either to reasonably believe that galanthamine should be administered transdermally for any particular therapeutic benefit or to reasonably expect that galanthamine could be administered transdermally with a likelihood of therapeutic success.

The prior art reasonably would have taught persons having ordinary skill in the art that galanthamine and physostigmine are both reversibly acting cholinesterase inhibitors and that both can be used to treat Alzheimer's Disease when administered in accordance with conventional wisdom in the art. However, the prior art of record would not have led persons having ordinary skill in the art to reasonably believe that active agents possessing some particular property or properties are more
or less likely to be administrable transdermally than active agents not possessing those properties with therapeutic

success. Persons having ordinary skill in the art with prior knowledge that certain kinds of active agents may be administered transdermally, might have been led to believe that chemically, physically, and/or structurally similar active agents could be administered in substantially the same manner. However, here the prior art has established therapeutic similarities only. We find no evidence of record that the common therapeutic properties exhibited by galanthamine and physostigmine would have reasonably suggested to persons having ordinary skill in the art that galanthamine could be administered transdermally with therapeutic success similar to that achieved when transdermally administering physostigmine, a compound which appears to be chemically, physically and structurally dissimilar to galanthamine.

4. Conclusion

We reverse the examiner's rejection of Claims 16-19 under 35 U.S.C. § 103.

5. Other Issues

The examiner should consider in the first instance the patentability of Claims 16-19 of this application in light of the subject matter claimed in Hille II, i.e., U.S. 5,700,480, patented December 23, 1997 (copy attached). Note the

following:

(1) the effective filing date of Hille II and this application;

(2) the inventive entity of Hille II and this application;

(3) the assignee of Hille II and this application;

(3) the reference to Opitz, K., DE 40 10 079 at column 1, lines 26-27, of Hille II; and

(4) the matrix polymers and matrix polymer additives Hille I describes at column 2, lines 50-66, of Hille I, U.S. 5,089,267, patented February 1991 (prior art to both Hille II and this application), for use in transdermal applicators.

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
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Richard E. Schafer) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND

) INTERFERENCES
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Appeal No. 94-4129
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APPENDIX

16. A transdermal applicator for the treatment of alcoholism comprising

a) an impermeable backing layer,

b) a polymer matrix connected to said backing layer and containing as active substance galanthamine (4a, 5, 9, 10, 11, 12-hexahydro-3-methoxy-11-methyl-6H-benzofuro[3a, 3, 2-ef] [2] benzazepine-6-ol), and

c) a pressure-sensitive adhesive element for fixing the applicator to the skin.